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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,380	11/28/2000	Vincent J. Miles	7960-147	9424

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EXAMINER
GUZO, DAVID

ART UNIT	PAPER NUMBER
1636	12

DATE MAILED: 05/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,380	Applicant(s) MILES ET AL.	
	Examiner David Guzo	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)[·] Responsive to communication(s) filed on *15 March 2002*.

2a)[·] This action is **FINAL**. 2b)[ ] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)[·] Claim(s) *3,8-10,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)[·] Claim(s) *18* is/are allowed.

6)[·] Claim(s) *3,8-10,17* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)[ ] The specification is objected to by the Examiner.

10)[ ] The drawing(s) filed on _____ is/are: a)[ ] accepted or b)[ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)[ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[ ] None of:

1.[ ] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No _____

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received

14)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11*.
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

DETAILED ACTION

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained for reasons of record in the previous Office Action (Paper #6) and for reasons outlined below.

Applicants traverse this rejection by asserting that applicants have demonstrated that the claimed composition inhibits *in vitro* translation of viral nucleic acid in a virus containing an IRES element and that no more is required to enable the claimed pharmaceutical composition. Applicants assert that as a composition claim, claim 17 does not recite method steps for treating an individual.

Applicant's arguments filed 3/15/02 have been fully considered but they are not persuasive. Applicants are claiming a **pharmaceutical** composition. A pharmaceutical composition is a medicament that must possess some therapeutic or otherwise beneficial activity in the subject to which the pharmaceutical composition is administered. Therefore, enablement issues regarding administering the composition, unpredictability of activity of compositions of the type claimed against diseases to be treated by the composition, the state of the art with regard to biological activities of the

pharmaceutical agents of the type claimed against the recited disease conditions, etc. must be considered because they are relevant to whether the claimed pharmaceutical compositions will have therapeutic activity in treating the disease(s) they are directed against. Applicants indicate that a demonstration of activity against viruses *in vitro* is sufficient to provide enablement of the composition claim. However, applicants present no data concerning activity of the claimed nucleic acid sequences against hepatitis A virus *in vitro* and applicants present no art recognized nexus between activity of the recited nucleic acid sequences in inhibiting translation *in vitro* of viral nucleic acids in viruses having IRES elements with activity of said nucleic acid sequences against hepatitis A virus. Applicants also present no art recognized nexus between the activity of the recited oligonucleotides in vitro and the activity the skilled artisan would expect to see *in vivo*, e.g. is the *in vitro* activity art recognized as being reasonably predictive of activity *in vivo*.

Applicants assert that the skilled artisan at the time of applicants' invention would have known how to develop the protocols and techniques to use the claimed oligonucleotide sequences and cite five articles (all published after the filing date) that applicants assert show that the specification would have been enabling at the time of filing. Applicants indicate that each of the cited references teach use of antisense oligonucleotides to inhibit hepatitis virus translation by targeting the 5' untranslated region of the virus. Applicants also assert that the two U.S. Patents cited have issued claims reading on pharmaceutical compositions comprising oligonucleotides and that one patent discloses no *in vivo* data.

In response, the examiner notes that the references cited by applicants disclose antisense molecules directed against a different, unrelated, virus (HCV, a flavivirus) rather than hepatitis A virus (a picornavirus). The relevance of antisense molecules targeted against an unrelated virus to the instant invention is unclear at best. It is noted that the non-patent reference cited by applicants (Zhang et al., published in 1999) makes clear the state of the art (as of 1999!) when the authors state that results of their research "...**suggests that antisense oligonucleotides may provide** (emphasis added) a novel approach to the control of HCV disease in patients." (p. 352, last paragraph). Clearly, Zhang et al., six years after the effective filing date of the instant invention, cautiously recite the mere potential for some future use of antisense oligonucleotides to treat HCV infection. This reference does not support applicants' assertion that the skilled artisan as of 1993 would have been able to use the claimed oligonucleotide pharmaceutical compositions to treat hepatitis A virus infection in patients. With regard to the U. S. Patents cited by applicants, it is noted that each patent application must be evaluated on it's own merits and that it is immaterial whether similar claims have been allowed to others (See *In re Giolitto*, 188 USPQ 645 (CCPA 1976) and *Ex parte Balzarini*, 21 USPQ2d 1892, 1897 (BPAI 1991).

With regard to the state of the art concerning treatment of hepatitis A virus in patients, Kaplan et al. (U.S. Patent 5,622,861, issued 4/22/97, see column 2) recites that there is no small animal model for studying hepatitis A virus infection, tropism or disease progression and that the large animal models are inherently limiting and constitute a significant barrier to development of effective treatments for hepatitis A

virus infection. Given the lack of animal models for hepatitis A virus infection, as disclosed by Kaplan et al., the relevance of applicants' *in vitro* data concerning successful oligonucleotide mediated inhibition of translation of viruses other than hepatitis A virus is unclear. Again, it is noted that applicants have presented no evidence of an art recognized nexus between applicants' *in vitro* results and the results which the skilled artisan would expect to see in use of the same molecules for treatment of humans for hepatitis A virus infection. Finally, it is noted that applicants have not specifically addressed the examiner's arguments (Wands factor analysis) made in the previous Office Action concerning the unpredictability of the art with respect to the use of antisense molecules for treatment of diseases, the poorly developed state of the art at the time of applicants' invention, etc.

Claims 3, 8-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have amended claim 3 to recite **a method for screening** for a nucleic acid capable of inhibiting translation of a nucleic acid sequence containing an IRES element from hepatitis A virus comprising **administering to an organism** a nucleic acid sequence complementary to at least a portion of said IRES. The amended claims read on an *in vivo* screening method using an organism that can be any single or multicellular organism such as a mammal or a human. The specification as originally

filed provides a written description for the claimed screening method in cell free extracts *in vitro* or in a cell *in vitro* but does not provide support for an *in vivo* screening method in multicellular organisms such as animals, mammals or humans. Redrafting the claim to recite "...administering to **a cell** *in vitro* said nucleic acid..." would be remedial.

Any rejections not repeated in this Office Action are withdrawn.

Claim 18 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

DAVID GUZO
PRIMARY EXAMINER

David Guzo
May 28, 2002